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# **Use of smartphone application to treat comorbidity depression with hypertension or diabetes I: a pilot study in Brazil and Peru**

Paulo Menezes, Julieta Quayle, Heloãsa Garcia Claro, Simone da Silva, Lena R. Brandt, Francisco Diez-Canseco, J. Jaime Miranda, LeShawndra N. Price, David C. Mohr, Ricardo Araya

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# Use of smartphone application to treat comorbidity depression with hypertension or diabetes I: a pilot study in Brazil and Peru

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## Abstract

**Background:** Depression is underdiagnosed and undertreated in primary health care. When associated with chronic physical disorders, it worsens outcomes. There is a clear gap in the treatment of depression in low- and middle-income countries (LMICs), where specialists and funds are scarce. Interventions supported by m-health technologies might help to reduce this gap. Mobile phones are widely used in LMICs offering potentially feasible and affordable alternatives for the management of depression among individuals with chronic disorders.

**Objective:** To explore the potential effectiveness of a m-health intervention to help people with depressive symptoms and comorbid hypertension and/or diabetes and to explore the feasibility of conducting large randomized controlled trials (RCTs).

**Methods:** Emotional Control (CONEMO) is a low-intensity psychoeducational 6-week intervention delivered via mobile phones assisted by a nurse for reducing depressive symptoms among individuals with diabetes and/or hypertension. CONEMO was tested in three pilot studies, one in São Paulo, Brazil, and two in Lima, Peru. Depressive symptoms were assessed using the PHQ-9 at enrollment and at six-week follow up.

**Results:** The three pilot studies included a total of 66 people. Most participants were female between 41 and 60 years old. There was a reduction in depressive symptoms as measured by PHQ-9 in all pilot studies. 38/66 participants reached treatment success rate (PHQ9<10): 13 from São Paulo, 13 from first Lima pilot and 12 from second Lima pilot study. The intervention, the app and the support offered by nurse and nurse assistants were well received by participants in both settings.

**Conclusions:** The intervention is feasible in both settings. Clinical data suggest that CONEMO might help to decrease participants' depressive symptoms. The findings also indicate that it is possible to conduct RCTs in these settings.

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## Original Manuscript

# **Use of smartphone application to treat comorbidity depression with hypertension or diabetes I: a pilot study in Brazil and Peru**

Menezes, PR; Quayle, J; Claro, HG; Silva, SA, Brandt, LR; Diez-Canseco, F; Miranda, J; Price, L; Mohr, D; Araya, R

## **Abstract**

### **Background**

Depression is underdiagnosed and undertreated in primary health care. When associated with chronic physical disorders, it worsens outcomes. There is a clear gap in the treatment of depression in low- and middle-income countries (LMICs), where specialists and funds are scarce. Interventions supported by m-health technologies might help to reduce this gap. Mobile phones are widely used in LMICs offering potentially feasible and affordable alternatives for the management of depression among individuals with chronic disorders.

### **Objectives**

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### **Methods**

Emotional Control (CONEMO) is a low-intensity psychoeducational 6-week intervention delivered via mobile phones assisted by a nurse for reducing depressive symptoms among individuals with diabetes and/or hypertension. CONEMO was tested in three pilot studies, one in São Paulo, Brazil, and two in Lima, Peru. Depressive symptoms were assessed using the Patient Health Questionnaire-9 (PHQ-9) at enrollment and at six-week follow up.

## Results

The three pilot studies included a total of 66 people. Most participants were female between 41 and 60 years old. There was a reduction in depressive symptoms as measured by PHQ-9 in all pilot studies. 38/66 (57.8%) participants reached treatment success rate (PHQ9<10): 13/21 (61.9%) from São Paulo, 13/21 (61.9%) from first Lima pilot and 12/24 (50.0%) from second Lima pilot study. The intervention, the app and the support offered by nurse and nurse assistants were well received by participants in both settings.

## Conclusions

The intervention is feasible in both settings. Clinical data suggest that CONEMO might help to decrease participants' depressive symptoms. The findings also indicate that it is possible to conduct RCTs in these settings.

**Keywords:** Depression, behavioral activation, m-health, pilot study, feasibility study, collaborative care, task shifting, mobile intervention, PHQ-9.

## Introduction

Depression is a leading cause for the burden of disease worldwide, with 4.4% of the world's population suffering from depression {World, 2017, Depression and other common mental disorders: global health estimates} [1, 2]. Depression is associated with poverty, low education and social exclusion, all of them more common in low- and middle-income countries (LMICs) [3-5].



Depression is also associated with physical chronic diseases and disability [3, 6]. The comorbidity of depression with other chronic diseases worsens outcomes in physical and mental conditions, decreases quality of life and increases the economic burden [3, 7-10].

In LMICs, people with depression are commonly underdiagnosed and undertreated [5]. One in every 27 people with depression receive treatment, and only 15% of these receive adequate care [11]. There are marked staff shortages in LMIC, especially of the more specialized resources such as psychiatrists, psychologists and psychiatric nurses [5, 12]. Much of this gap has to be covered through the strategy of task shifting or transferring responsibilities for the care of the mentally ill to a lower cadre of health workers [13]. However, task shifting also requires resources to identify, train, and supervise non-specialized health care workers or lay counsellors, which is frequently not available, making it difficult to scale it up in many environments. Digital mental health technologies, which can provide treatment to patients via apps, and connect patients to a care coordinator, can simplify care coordination tasks, reducing the amount of training, thereby providing a more scalable process [14]. There is a growing body of evidence that mobile interventions for common mental health problems such as depression and anxiety, delivered through an app can be effective in reducing symptoms. Whether they are more effective when accompanied by support from a coach or care coordinator than stand-alone solutions is still controversial [15].

The Latin America Treatment & Innovation Network in Mental Health (LATIN-MH) seeks to develop and test a blended intervention for depression and comorbid chronic health problems, such as hypertension and/or diabetes. We developed CONEMO (“Emotional Control”), a low-intensity psychoeducational 6-week intervention delivered via mobile phones assisted by a nurse for reducing depressive symptoms among individuals with diabetes and/or hypertension.

The intervention aims to reduce depressive symptoms among patients with comorbid diabetes and/or hypertension recruited in different health service units in São Paulo (Brazil) and Lima (Peru). Therefore, the focus of this project is on providing patients tools through smartphones, with low-

intensity support that can be provided with minimal time by nurses or nurse assistants, who are available in the clinics but have no specialized training in mental health. These professionals receive specialized supervision provided by the study staff to perform their tasks. This intervention is unique in LMICs in terms of using a technological platform and integrating the care of mental and physical chronic conditions [16].

This pilot study aimed to:

- 1) Explore the potential effectiveness and feasibility of using the CONEMO intervention to help people with hypertension and/or diabetes and comorbid depressive symptoms;
- 2) Test recruitment strategies to estimate how many participants should be screened to reach our target sample for fully powered Randomized Controlled Trials (RCTs); and
- 3) To assess acceptability and satisfaction of patients with the CONEMO intervention.

## Methods

### Study Design, Settings and Participants

We conducted three pilot studies during 2015-2016: one in São Paulo, Brazil, and two in Lima, Peru. São Paulo is the largest city of Brazil, with 11.2 million inhabitants [17]. Brazil offers universal health coverage to its population with primary care playing a key role. The Family Health Care Strategy (FHCS) aims to provide primary care close to where inhabitants live through family health teams composed of one family or general physician, one nurse, two nurse assistants, and five to six community health agents. [18]. Currently there are more than 43,000 Family Health Teams covering 65% of the total population in the country and 40% of the population in the city of São Paulo [19]. A large survey estimated that approximately 10% of the population in São Paulo fulfilled criteria for major depression in the past 12 months, with 80% presenting moderate to severe depression [20]. A recent census indicated that Brazil has currently 5 psychiatrists per 100,000

inhabitants, but the majority work only in the private sector.

Lima, the capital of Peru, has approximately 9 million inhabitants, one third of the total Peruvian population[21]. The prevalence of depression has been estimated as 17,5% [22]. In Peru, health care is offered both in public and private sectors, from primary to tertiary-care level, and although the current mental health reform is aiming at shifting mental health care towards a community approach, the majority of mental health care is still restricted to tertiary-care level facilities [23]. The Peruvian health care system is administered by different entities: the Ministry of Health (MINSA) (covering 60% of the population), EsSalud which is a social and health insurance for employees (30% coverage), and armed forces, police and private sector (covering the remaining 10%) [24]. In Peru there are 0.6 psychiatrists per 100,000 inhabitants, well below the average for LMICs.

In São Paulo we conducted the pilot study with four teams of two FHCS clinics. In Lima the first pilot study took place in the endocrinology and cardiology outpatient consultation area of a tertiary-level hospital from the MINSA, whilst in the second pilot patients were recruited in two primary care health centers, mostly in the elderly adult consultation programs, where people with NCDs are monitored, at EsSalud. Participants were eligible according to the following criteria:

Inclusion criteria:

1. Aged 21 or over;
2. Hypertension and/or diabetes;
2. Depressive symptoms, evaluated by the PHQ-9 (score  $\geq 10$ );
3. Self-reported reading ability in Portuguese (São Paulo) or Spanish (Lima);

The exclusion criteria were:

1. Psychosis symptoms detected by a 5-item screening questionnaire;
2. Pregnancy (self-reported);
3. High suicidal risk detected by a positive answer in the item 9 of the PHQ-9 followed by a

protocol to assess suicidal risk [Suicide Risk Assessment Protocol (S-RAP)]; and

4. Cognitive impairment detected by a 4-item questionnaire.

We used convenience samples in the three pilot studies. We envisaged that with 20 participants in each pilot we would be able to achieve the aims proposed.

## Measurements

We collected information about socioeconomic and demographic characteristics, depressive symptoms, suicidal ideation, presence of psychosis symptoms, cognitive impairment, quality of life, adherence to medical treatment, and disabilities (Table 1).

Table 1: Description of instruments used in the pilot studies, time of application, and purpose. São Paulo, Brazil, and Lima, Peru.

Instrument	Time	Purpose
First Informed Consent (S1)	Pre-Screening	Introduction of the study and obtaining consent for screening
PHQ-2/PHQ9/S-RAP (S2)	Screening	Assessment of depressive symptoms and suicidal ideation
Second Informed Consent (B1)	Before baseline	Consent to the study
PHQ-9	Screening/Risk Assessment (1 and 3 weeks)/Follow up	Full screening for depressive symptoms
S-RAP	Screening/Risk Assessment (1 and 3 weeks)/Follow up	Assess Suicidal Risk
PSQ	Screening	Assess the presence of psychosis
CSI-D	Screening	Evaluate cognitive impairment
Demographic and	Baseline	Information about participants

Socioeconomic characteristics		socioeconomic and family background
Clinical data	Baseline	Medical history
WHODAS-II	Baseline/Follow-ups	Assess functional disability
EQ-5D	Baseline/Follow-ups	Asses quality of life
Morisky Medication Adherence scale	Baseline/Follow-ups	Evaluate self-referred medication adherence

To explore the potential effectiveness of CONEMO intervention, we used the Patient Health Questionnaire (PHQ-9) as the main measure of outcome [25]. We applied the PHQ-9 at baseline and at the end of the 6-week intervention to assess severity of depressive symptoms.

To rule out the presence of psychotic symptoms we used the Psychosis Screening Questionnaire – PSQ [26], to assess cognitive impairment we used the Community Screening for Dementia CSI-D [27], and to estimate quality of life the EuroQoL EQ-5D[28]). Among those taking medication, we assessed adherence to medication treatment with the Morisky Medication adherence scale [29]. Disabilities were assessed with the World Health Organization Disability Assessment Schedule - WHODAS-II[30].

We also used data from participants captured automatically by the CONEMO system in order to monitor patients' progress, including completion of sessions, intervals between accessing sessions, or sessions missed. We collected information from participants about the acceptability and satisfaction with CONEMO app and the dashboard, through a questionnaire using a Likert scale of five points at the end of the pilot study, where 1 is *disagree* and 5 is *agree*.

### CONEMO Intervention

We tested an intervention that could be delivered in existing general medical care settings by available local personnel. The choice of a psychological intervention as the main component relates

to the public health need for these approaches in most LMICs. CONEMO is a smartphone-delivered intervention, supported by a Nurse Assistant or a Nurse, using a task-shifting model, as recommended by the World Health Organization [13, 31]. CONEMO consists of 18 behavioral activation sessions, delivered over six weeks (three sessions per week). As part of the behavioral activation program, CONEMO aims at increasing daily life activities, especially pleasant ones, healthy ones and tasks, as well as providing further information and health self-care messages, increasing motivation and improving adherence to medication (Figure 1). Participants received a device from the project with the CONEMO application installed, for use during the 6-week program, returning it to the responsible nurse after that period.

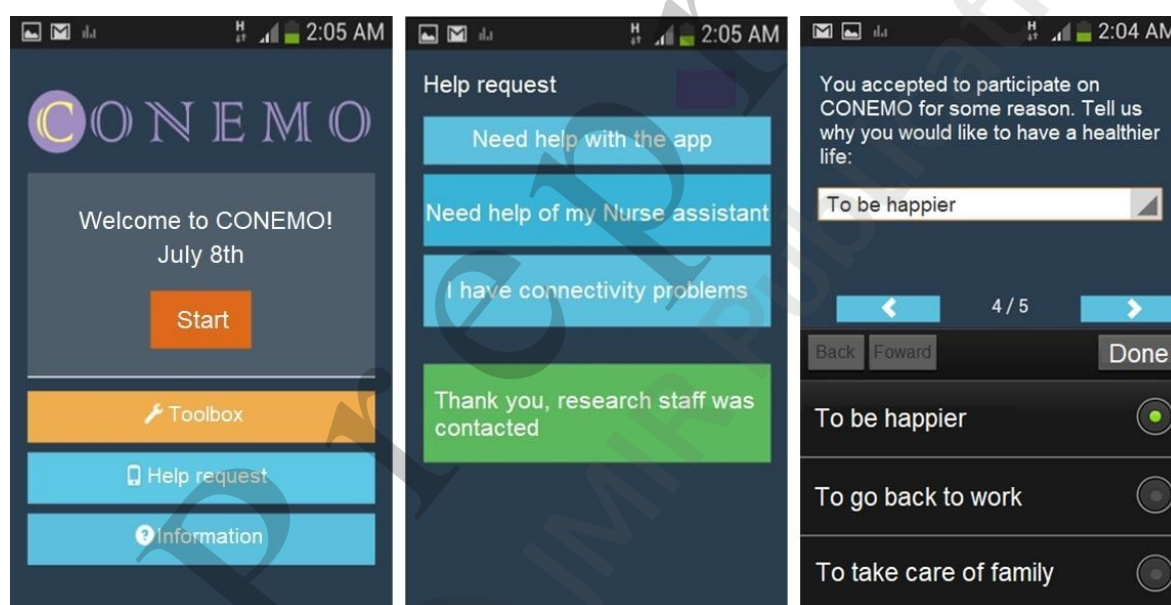


Figure 1: CONEMO app screenshots

The tasks of the nurse/NA were: 1) an initial contact by phone to schedule a training session for the participant; 2) a face-to-face training session to introduce the CONEMO app; 3) a monitoring call after week one to answer possible queries from participants and to reinforce motivation to participate; 4) a monitoring call after week four with the same objectives as above; 5) a phone call to schedule the closing meeting; 6) a final face-to-face appointment with the participant to finish the

intervention and return the smartphone. Nurses/NAs received weekly face-to-face supervision from research clinical psychologists.

## Data analysis

To test recruitment strategies, we analyzed data gathered during the process of recruiting and enrolling participants (Aim 2). The comparison of participants' PHQ-9 scores at baseline and at follow-up allowed a preliminary assessment of potential effectiveness (Aim 1), and the number of sessions completed and ratings on the satisfaction with the CONEMO intervention gave us an insight into the acceptance of the CONEMO intervention (Aim 3).

The main outcome measure was patients' PHQ-9 scores at the end of the 6-week intervention. We considered patients had recovered when the PHQ-9 score at follow-up was  $<10$ . Secondary outcomes, such as disability levels, quality of life, and adherence to medication were also examined at the end of the studies. Descriptive statistics were also used to assess participants' perceptions at the end of the study. We conducted all data analysis using STATA 11 [32].

## Ethical Considerations

The pilot studies were approved by local IRBs and the U.S. National Institute of Mental Health (NIMH) Data and Safety Monitoring Board. Participants consented to participate in the study and interviews took place after collecting the participants' signatures on informed consent forms. All investigators and research assistants involved in the data collection and analysis completed ethics and human research good clinical practices training before starting their activities in the project.

## Results

### Assessment of recruitment strategy

We carried out one pilot study in São Paulo and two pilot studies in Lima. In São Paulo, four nurses from the two participating FHCS clinics were responsible to support the CONEMO intervention for participants recruited into the study. In the first pilot in Lima we employed a nurse to support the delivery of the intervention, whereas in the second pilot study in Lima we worked with six nurses employed by two public health care facilities. We included 66 patients in the three pilot studies after approaching 793 people (Figure 2). Of 216 subjects approached in São Paulo, 21 (10%) were included in the pilot study. In the two pilot studies in Lima we approached 577 subjects to include 45 (8%) participants, 21 in the first and 24 in the second pilot studies. To recruit participants we spent 30 days in the field in São Paulo, 21 days in Lima's first pilot study and 24 in Lima's second pilot study. Most participants were women between 41-60 years old (Table 2). In São Paulo, participants had lower educational level than in Lima.



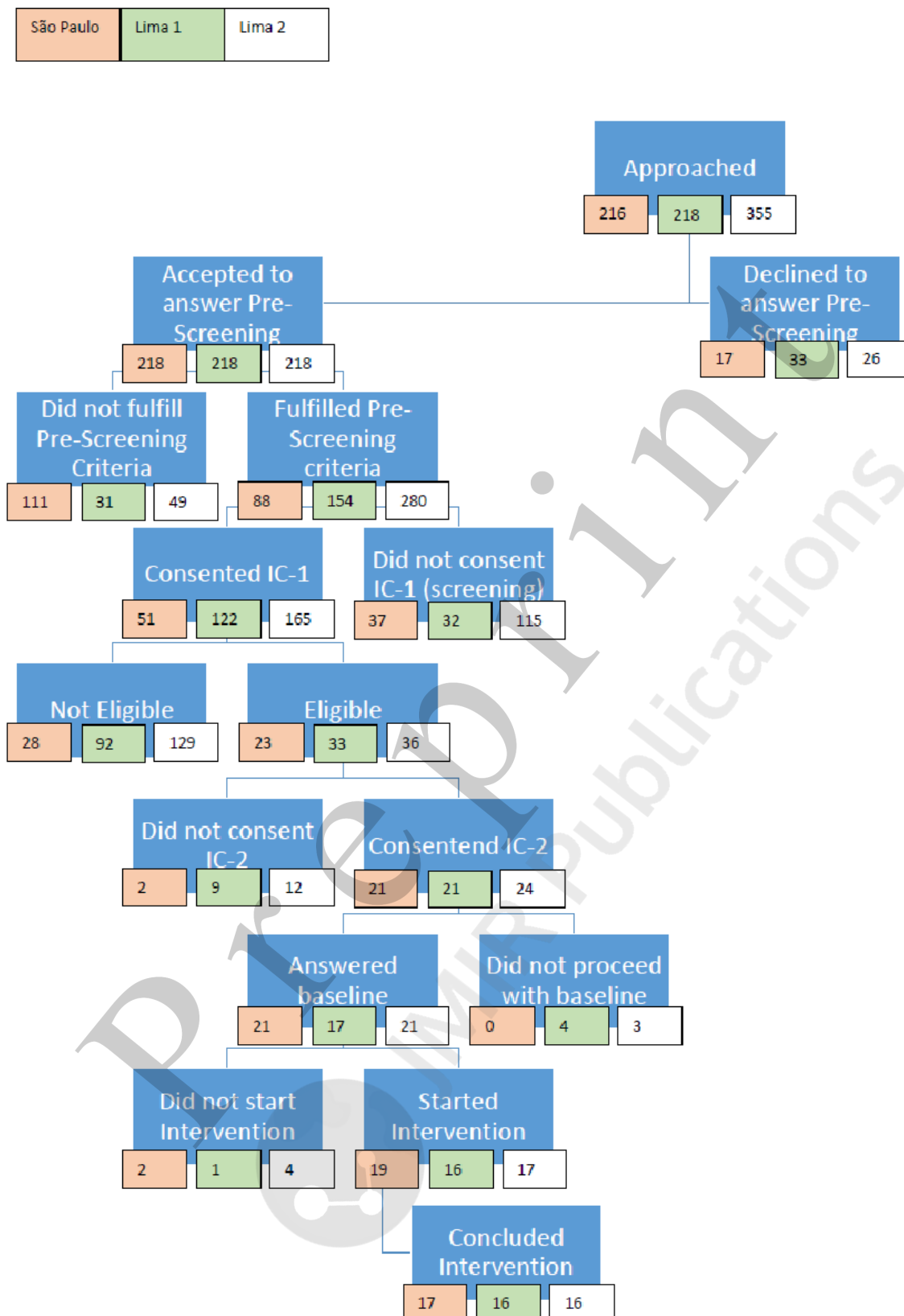


Figure 2:

Flow chart of recruitment and intervention in Lima and Sao Paulo

Table 2: Socioeconomic and demographic characteristics of participants included in the pilot studies in São Paulo, Brazil and Lima, Peru.

	São Paulo n = 21 (%)	Lima - pilot 1 n = 21 (%)	Lima - pilot 2 n = 24 (%)	Total n=66 (%)
Age				
21-40	3 (14.3)	0	1 (4.2)	4 (6.1)
41-60	11 (52.4)	13 (61.9)	11 (45.8)	35 (53.0)
>=61	7 (33.3)	8 (38.1)	12 (50.0)	27 (40.9)
Gender				
Male	5 (23.8)	8 (38.1)	6 (25.0)	19 (28.8)
Female	16 (76.2)	13 (61.9)	18 (75.0)	47 (71.2)
Chronic disease				
HBP	14 (66.6)	1 (4.8)	9 (37.5)	24 (36.4)
DM	1 (4.8)	12 (57.1)	6 (25.0)	19 (28.8)
HBP + DM	6 (28.6)	8 (38.1)	9 (37.5)	23 (34.8)
Educational Level				
Primary School	12 (57.1)	3 (14.3)	4 (16.7)	19 (28.8)
High school	6 (28.6)	8 (38.1)	5 (20.8)	19 (28.8)
Technical course	3 (14.3)	4 (19.0)	7 (29.2)	14 (21.2)
University/Postgraduate	0	2 (9.5)	5 (20.8)	7 (10.6)
(missing )	0	4 (19.0)	3 (12.5)	7 (10.6)
Income (Brazilian Minimum Wage)				
0-4 minimum wage	14 (66.6)			14 (21.2)
more than 4 minimum wage	7 (33.3)			7 (10.6)
Income Peru (Soles)				
0 - 1500		9 (42.9)	7 (29.2)	16 (24.2)
More than 1500		7 (33.3)	12 (50.0)	19 (28.8)
Do not know / Did not answer		5 (23.8)	5 (20.8)	10 (15.2)

HBP: High Blood Pressure (Hypertension); DM: Diabetes Mellitus

### Potential effectiveness and feasibility of CONEMO intervention

At the six-week follow up, there was 1 (4.8%) loss to follow-up in Sao Paulo, 6 (28.6%) in the first and 8 (33.3%) in the second Lima pilot studies. Among participants who completed follow-up assessments, at baseline 11 out of 20 (55.0%) had moderately severe or severe symptoms of depression in Sao Paulo (Figure 3). In Lima, none had severe symptoms at baseline and 8 out of 31 (25.8%) had moderately severe symptoms. At follow-up assessment, 13/20 (65.0%) participants had recovered from depression (PHQ-9<10) in Sao Paulo, 13/15 (86.7%) in the first Lima pilot study and 12/16 (75.0%) in the second Lima pilot study (Figure 3). Only two (12.5%) participants in Lima's second pilot study worsened their level of depressive symptoms. Six participants (30%) presented mild suicide risk at baseline in Sao Paulo, whereas in Lima none of the participants presented suicide risk. In the follow-up assessments of the three pilot studies no participant presented suicide risk.

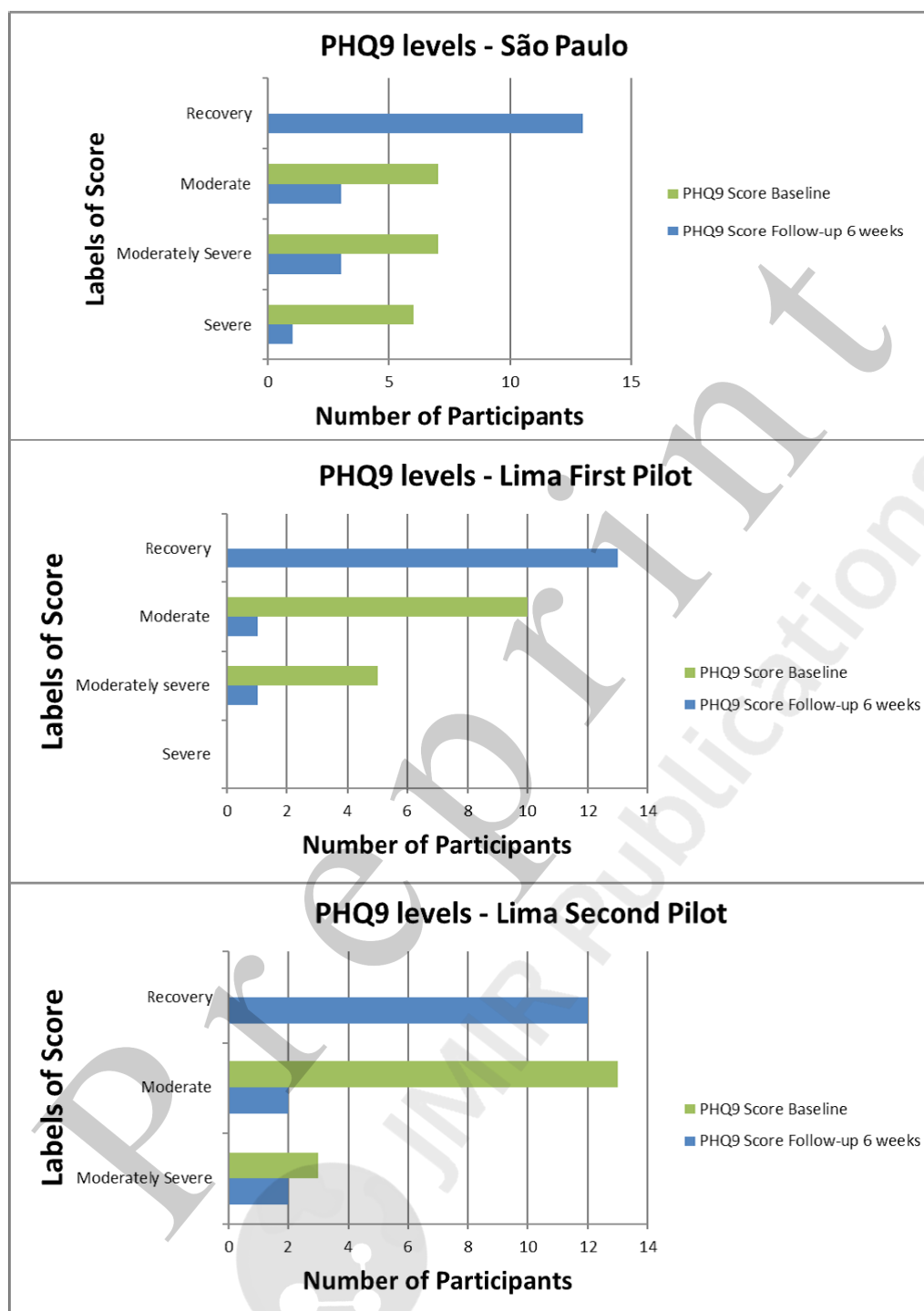


Figure 3: Severity of depressive symptoms at baseline and 6-week follow-up, according to PHQ-9 scores, for the three pilot studies (São Paulo, Brazil, and Lima, Peru).

There was a trend for improvement in self-reported adherence to medical treatment in São Paulo from baseline to 6-week follow-up (Table 3). No clear trends in adherence to medication were noted in Lima. In São Paulo and Lima all participants presented some level of functional disability at baseline, with more than 50% presenting moderate or severe functional disability. In all pilot studies, there was a trend towards a reduction in levels of functional disability at the follow-up assessments (Table 3). Regarding quality of life, we observed small inconsistent variations on EQ-5D scores from baseline to 6-week follow-up (Table 3).

Table 3: Medication adherence, functional disability, and quality of life during baseline and at 6-week follow-up in São Paulo, Brazil and Lima, Peru.

	São Paulo				Lima - pilot 1				Lima – pilot 2			
	(N=20 <sup>a</sup> )				(N=15 <sup>a</sup> )				(N=16 <sup>a</sup> )			
	Baseline		6w - FUP		Baseline		6w – FUP		Baseline		6w - FUP	
	N (%)				N (%)				N (%)			
MORISKY MEDICATION ADHERENCE SCALE												
High adherence (0 points)	2	10%	5	25%	2	13%	1	7%	7	44%	1	6%
Medium adherence (1-2 points)	12	60%	13	65%	8	53%	11	73%	6	38%	11	69%
Low adherence (3-4 points)	6	30%	2	10%	5	33%	3	20%	3	19%	4	25%
WHODAS												
No Disability	0	0%	2	10%	0	0%	1	7%	0	0%	0	0%
Mild disability	9	45%	10	50%	5	33%	9	60%	7	44%	9	56%
Moderate disability	8	40%	5	25%	7	47%	5	33%	7	44%	7	44%
Severe disability	3	15%	3	15%	2	13%	0	0%	2	13%	0	0%
EQD-5												
Problems to walk	10	50%	11	55%	10	67%	7	47%	7	44%	5	31%

		%										
Problems washing or dressing	9	45	5	25%	3	20%	2	13%	1	6%	0	0%
Problems with performing usual activities	9	45	9	45%	8	53%	4	27%	5	31%	5	31%
Moderate or extreme pain / discomfort	14	70	16	80%	14	93%	11	73%	13	81%	11	69%
Moderate or extreme anxiety / depression	17	85	15	75%	7	47%	7	47%	12	75%	8	50%
<sup>a</sup> N = number of participants with follow up after 6 weeks.												

Access of participants to the CONEMO sessions decreased progressively overtime in the Sao Paulo and in the 2<sup>nd</sup> Lima pilot study (Figure 4), whereas in the 1<sup>st</sup> Lima pilot study access started to decrease only after 4 weeks of the intervention. Proportions of completion of sessions were 70% in São Paulo, and 88% and 58% in the first and the second pilot studies in Lima, respectively. In São Paulo, 87% of the participants accessed all first 6 sessions, whereas 95% and 76% did so in the 1<sup>st</sup> and 2<sup>nd</sup> pilot studies in Lima, respectively. Sixty-nine percent of participants in São Paulo, and 91% and 50% in Lima accessed sessions 7 to 12. Adherence decreased for sessions 13 to 18, with 55% in São Paulo, 80% and 48% in the 1<sup>st</sup> and 2<sup>nd</sup> studies in Lima, respectively.

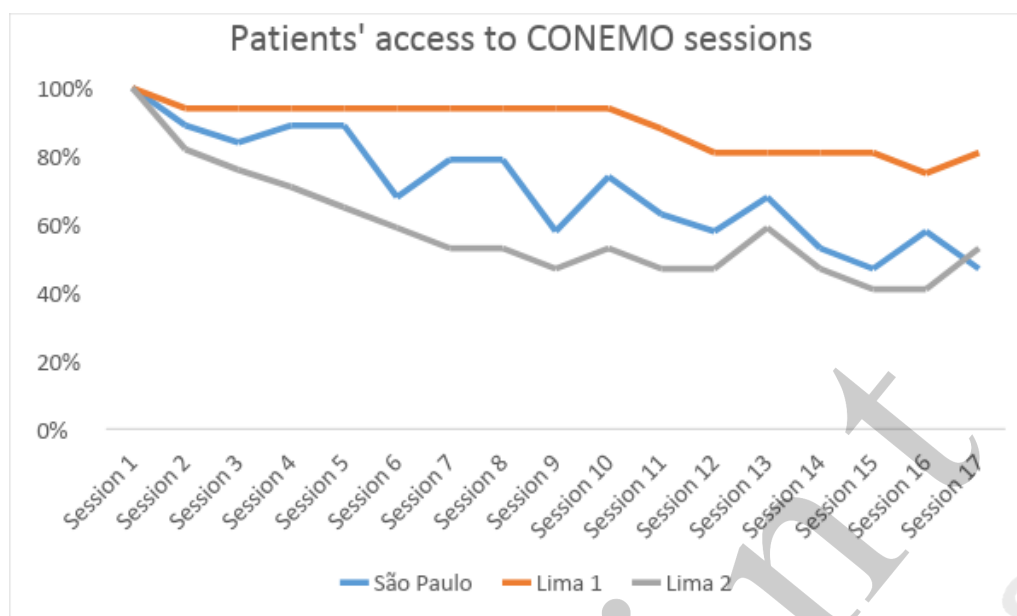


Figure 4 – Proportion of participants who accessed each of the CONEMO app sessions in the pilot studies in São Paulo, Brazil and Lima, Peru.

The CONEMO app (participant interface) worked adequately during the trial, despite some connectivity issues when receiving information on participants' performance. These issues did not affect the intervention or data collection.

We collected data on acceptability and satisfaction with CONEMO from 20 participants in São Paulo, 15 in Lima's first pilot and 16 in Lima's second pilot. The evaluation of the intervention by participants was generally positive: all mean ratings were above 3.5 points (maximum of 5 points), both in São Paulo and Lima. Patients considered that the objectives were attained and that the intervention helped their physical and mental health and to get organized. In their opinion the duration of the intervention, the amount of contacts with the nurse/NA and the training received were adequate (Table 4).

Table 4: Evaluation of participants regarding CONEMO intervention in the pilot study in São Paulo, Brazil and Lima, Peru.

<b>Intervention evaluated</b>	<b>aspects</b>	<b>São Paulo Average grade</b>	<b>Lima 1 Average grade</b>	<b>Lima 2 Average grade</b>
Helped with physical health		4.1	4.0	3.8
Helped with mental health		4.4	4.4	4.3
Helped having the will to do things		3.9	4.3	4.3
Helped to get organized		3.6	4.3	4.3
Count on Nurse Assistant/nurse		4.5	4.1	4.1
Nurse Assistant/nurse helped		4.4	4.3	3.8
Number of contacts		4.1	3.6	3.2
Training quality		4.1	3.7	3.1
Intervention duration		4.1	2.8	2.9
Achievement of objectives		4.1	4.2	4.2
Satisfaction with results		4.3	4.4	4.3
Would indicate to a friend		3.6	4.6	4.5

Participants considered the CONEMO app easy to use, were able to access videos and other resources included in the app and thought the size of fonts and layout of the app was appropriate (Table 5). They also assessed the role of nurses/NAs in the task shifting strategy proposed in the CONEMO intervention. They considered training, procedures and availability of nurses/NAs as sufficient or good. Around 90% of the participants in all pilots considered important to have nurses/NAs support.

Table 5: Evaluation of participants regarding technological aspects of CONEMO app used during the pilot studies in São Paulo, Brazil and Lima, Peru.

Item	São Paulo Average grade	Lima Average grade	Lima 2 Average grade
Easy to use	4.4	4.3	3.8
Usefulness	4.6	4.7	4.4
Adequacy of frequency of sessions	4.3	3.3	3.9
Content interesting	4.4	4.6	4.5
Video quality	4.4	4.6	4.4
Sound quality	3.9	4.6	4.3
Choices presented	4.1	4.6	4.5
Training session	4.3	4.0	4.3
Reminders	3.6	3.0	4.3

## Discussion

The main aim of the present pilot study was to explore the feasibility and potential effectiveness of the CONEMO intervention for depressed people with co-morbid hypertension or



diabetes. We also wanted to assess the feasibility of undertaking fully powered RCTs to test the effectiveness of this intervention. We found that patients were able to use the CONEMO app, that they tended to show improvement in the severity of depressive symptoms by the end of the intervention, and that they were satisfied with the intervention. Our results are encouraging and suggest that the intervention is feasible and potentially effective with this population.

In order to carry out RCTs we needed to ensure that we would be able to recruit participants in the numbers needed. On average, out of each 13 participants screened we were able to include one eligible participant in the study. In São Paulo and Lima recruitment took place in primary health care units and additionally in the outpatient consultation areas of a public hospital in the first pilot study in Lima, with patients presenting different conditions apart from hypertension and diabetes. In both sites, many participants were unable to read or write. As a result, it was necessary to pre-screen twice as many patients than we first anticipated in order to reach the numbers we had planned for each pilot study. This information allowed us to prepare a more realistic recruitment strategy and plan.

The instruments and measures were well understood by participants, and research assistants also provided positive feedback on their use. The outcome measures seemed sensitive to change and allowed a useful characterization of the study sample. The research assistants did not refer problems from the participants in understanding the instructions or questions included in the study. Since only one participant showed cognitive impairment and/or psychotic symptoms in the screening, the assessment of these conditions may not be needed in the full trials. This will decrease the time taken for screening interviews, also reducing costs for running the trials.

Overall, there was a noticeable trend in all pilot studies for a reduction on depressive symptoms over time, as measured by the PHQ-9. Our approach was categorical, using PHQ-9 cut-off points to decide on caseness and severity. The proposed measure of clinical success, having a PHQ-9 score  $\leq 9$  at follow up (recovery), was considered a stringent but good measure. All our estimates, though, need to be taken with caution as this pilot study was not powered to detect any statistically

significant changes.

Other secondary measures of success of the intervention also yield some results in the expected direction. Disability levels and medication adherence seemed to improve by the end of the intervention. This trend was not as clear for the quality of life measure (EQ-5D).

The study also found that participants were satisfied with the intervention and the nurse/NA support. Other studies have also shown benefits in the use of a collaborative care and task shifted approaches in the treatment of depression [33-35]. Participants found the CONEMO app useful, easy to use, and with interesting content. There was a decrease in adherence to the sessions over time, which is consistent with a large majority of digital mental health interventions. This suggests a need to review the content and organization of the sessions before the start of the RCTs. Changes should include shortening sessions, making language simpler, and adding more video material. Reviewing our strategy for persuasive design could also improve longer term adherence, such as including more tailoring and personalization, improving the quality automated notifications (e.g. positive reinforcement for engagement), and leveraging contact with the nurse coordinator. We are hopeful that these changes will improve session adherence in the RCTs.

## Strengths and Limitations

To the best of our knowledge, this is the first study that pilot tested a mobile intervention for symptoms of depression among individuals with chronic conditions in two settings of middle-income countries of Latin America. Our samples were small, so the pilot studies were not powered to test the efficacy of the intervention, but our results were in the predicted direction, and the proportions of treatment success in each sample are useful to calculate full trial sample sizes. We found that many potentially eligible participants could not participate because of difficulties to read or write. This could potentially affect the generalizability of the results. However, with the increasing literacy trend

in younger generations in Latin America, these difficulties will decrease and more and more people will be able to benefit from similar apps in the near future.

## Conclusions

The technological system CONEMO seems feasible to use in these settings with different languages to help patients with diabetes or hypertension and co-morbid depressive symptoms. The results from the three pilot studies are promising and support the implementation of fully powered trials. CONEMO intervention will be one of the first evidence-based mobile interventions tested in large samples in two different settings in LMICs.

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## Conflicts of Interest

None declared.

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## Supplementary Files

## Figures

**Figure 3.** Severity of depressive symptoms at baseline and 6-week follow-up, according to PHQ-9 scores, for the three pilot studies (São Paulo, Brazil, and Lima, Peru).

